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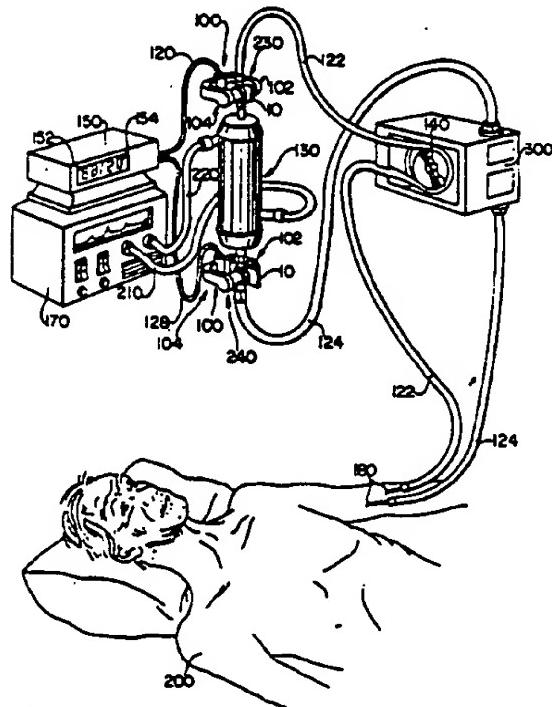
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(54) Title: SYSTEM AND METHOD FOR NONINVASIVE HEMODYNAMIC MEASUREMENTS IN HEMODIALYSIS SHUNTS

## (57) Abstract

Access recirculation in a shunt is determined quantitatively by a method in which a standard solution, such as saline, is injected into a patient's (200) bloodstream upstream of the shunt. At a point in the access line, a photometric measurement is conducted of the change in hematocrit ( $\Delta H$ ) with respect to time. Electronic circuitry (150) receives signals from the detector (100), compares the integrated area of  $\Delta H$  with respect to time of the standard solution initially flowing through the access of the recirculated solution, and provides display of recirculation (152).



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## SYSTEM AND METHOD FOR NONINVASIVE HEMODYNAMIC MEASUREMENTS IN HEMODIALYSIS SHUNTS

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### CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to U.S. Provisional Application No. 60/029,587, filed October 23, 1996.

### FIELD OF THE INVENTION

This invention relates to systems and methods for noninvasively measuring hemodynamic access, access recirculation and blood flow measurements during hemodialysis. More particularly, the present invention relates to noninvasive spectrophotometric systems and methods for quantitatively measuring the shunt (access) recirculation, the access blood flow rate, the dialysis machine blood flow rate and the volumes of priming fluids required by the hemodialysis tubing lines.

15

### INTRODUCTION

Modern medical practice utilizes a number of procedures and indicators to assess a patient's condition especially in the dialysis setting. Hemodialysis is a process wherein an artificial kidney is required to function in the place of the patient's normal kidney in order to remove certain biologic waste products. When the human kidney no longer functions correctly removing waste products such as urea, potassium, and even excess water, blood must be removed from the patient via blood tubing lines and filtered through an artificial kidney or dialyzer. In this process blood is passed through the dialyzer,

cleansed, then returned to the normal circulatory system of the patient. Access to the patient's circulatory system is achieved through the use of a surgically implanted shunt or fistula. This "access site" is typically located in the arm, leg, or neck of the patient. Typically needles are placed into this "access" in such a way as to facilitate the easy removal of blood on the "arterial" or upstream side of the dialyzer and typically return the purified blood downstream of the first needle placement on the "venous" side. Unfortunately, in many cases the fistula, or shunt, will clot or "stenos" over time. This results in decreased blood flow through the access which ultimately necessitates either angioplasty or a surgical replacement of the shunt. As the shunt ceases or "clots off" part 5 of the purified dialyzed blood is forced to flow back into the arterial withdrawal site and, hence, recirculates only to be dialyzed again; this is termed "access recirculation". As 10 this recirculation of purified blood continues, the rest of the patient's circulating blood is not adequately cleansed and, hence, an inadequate delivery of the dialysis dosage is provided to the patient.

15 Therefore, because of the possibility of inadequate dialysis dosage due to this direct recirculation of purified blood back to the withdrawal site, various techniques and methods have been designed to determine:

- 1) The degree or percentage of access recirculation;
- 2) The actual blood flow rate in the shunt per se; and
- 20 3) The dialyzer blood flow rate itself.

Medical professionals desire to know these three parameters not merely qualitatively, but quantitatively in order to determine the presence and degree of clotting

or stenosis. These parameters are desired to predict when the access is beginning to fail and to determine the need for access revision by surgery. Blood flow, Q, measured by the so-called Ficke dilutional techniques, has been described by A.C. Guyton, Textbook of Medical Physiology, Sixth Edition, pg. 287, 1981, wherein Q equals the volume of the  
5 injected diluent divided by the mean concentration of the diluent times the duration of the passage of the diluent through the vessel. A dilution curve is obtained by continuously monitoring changes in a given physical parameter of the blood over the time period of the injection. The change in the concentration of either the diluent (or the media) is measured over time.

10 Hester, R.L. et al., American Journal of Kidney Disease 20:6, 1992, pp. 598-602, have shown that when the dialyzer blood lines are reversed, enhanced blood recirculation occurs. Krivitski, in European patent application number WO9608305A1, indicates that blood line reversal (causing forced recirculation) allows for the determination of the actual blood flow in the shunt.

15 One method of measuring access blood flow utilizes color coded duplex sonography. However, this technique is expensive. It involves highly trained professionals and the measurements suffer from operator error. The limitations due to variations in the blood vessel diameter and even the Doppler flow angle complicate this measurement.

20 Another method involves injection of a saline solution intravenously and recording optical detecting the change in the intensity of light passed through a conduit at a point upstream from the injection point (U.S. Pat. No. 5,312,550).

Another technique involves injecting saline boluses into the arterial and venous dialyzer tubing lines and measuring the change of ultrasound velocity (U.S. Pat. No. 5,453,576). This technique is sensitive to changes in temperature, plasma protein levels, and other intrinsic factors that change the density of the blood. Of more significance, 5 however, is that the measurements of the absolute ultrasound velocity changes are influenced not only by the intrinsic blood factors, but also by the unknown mechanical properties of the tubing line per se. In order to compensate for those intrinsic and extrinsic physical problems an additional calibration injection of saline is generally required in the opposite tubing line, whether arterial or venous, thereby producing 10 relative changes in the degree of dilution that occurs due to the saline bolus. Hence, the unknown ultrasound characteristics of the tubing line and other physical, dimensional characteristics can be minimized.

The present standard measurement for access recirculation requires three blood urea nitrogen samples from the patient while on dialysis. However, in addition to the 15 blood samples required from the patient, nursing time, laboratory costs, and appropriate blood flow rates must be maintained during the actual sampling procedure to assure correct urea nitrogen measurements.

Thus, there remains a need for systems and methods for noninvasively and quantitatively determining a patient's hemodynamic access blood flow and blood 20 recirculation parameters.

## OBJECTS OF THE INVENTION

Thus, it is an object of the present invention to provide a system and method for noninvasive access hemodynamic monitoring that requires minimal nursing time and no discreet blood sampling.

5 It is another object of the present invention to provide a system and method for the display of both immediate and continuous visual information regarding the saline dilutional hemodynamic access data.

10 It is yet another object of the present invention to provide repeatable and reliable systems and methods for the noninvasive determination of the hemodynamic access flow properties under varying conditions including: different ultrafiltration rates, patient postures, tubing types and dimensions, and even different dialyzer membranes and dialysis delivery systems.

15 Another object of the present invention is to provide a means and method of quantitatively determining the volumetric blood flow rate actually passing through the dialyzer,  $Q_i$ .

Another object of the present invention is to present the dilutional concentration-time curves to the operator by visual, real-time display means.

20 Still another object of the present invention is to provide a system and method which can provide immediate and quantitative determination of the actual volume of fluid necessary to prime the dialyzer circuit.

It is likewise another object of the present invention to provide a system and method for determining the access blood flow and access recirculation that does not

require the injection of saline. For example, by changing the ultrafiltration rate (UFR) or dialyzer blood flow rate. It is another object of the present invention to provide a system and method for measuring dialyzer blood flow parameters.

These and other objects and advantages of the invention will become more fully apparent from the description in the claims which follow or may be learned by the practice of the invention.

### SUMMARY OF THE INVENTION

In one aspect of the present invention, access recirculation in a shunt is determined quantitatively by a method in which a standard solution, such as a saline solution, is injected into the patient's bloodstream at a point upstream of the shunt. At a point in the access line, a photometric measurement is conducted of the change in hematocrit ( $\Delta H$ ) with respect to time. Electronic circuitry receives signals from the detector and compares the integrated area of  $\Delta H$  with respect to time of the standard solution initially flowing through the access and of the recirculated solution and provides a nearly instantaneous display of the amount of access recirculation.

In another aspect of the present invention, the access recirculation and/or access blood flow are quantitatively determined without injecting a solution into the bloodstream. In this aspect the extent of access recirculation and/or access blood flow is determined quantitatively by a method in which the dialyzer blood flow rate or the ultrafiltration rate (UFR) is changed and the corresponding change in concentration of a blood constituent is measured. In this technique, the concentration of a blood

constituent is measured as a function of dialyzer blood flow rate or UFR and electronic circuitry converts these measurements into quantitative determinations of access recirculation and/or access blood flow that can be displayed nearly instantaneously. In a preferred embodiment the measured blood constituent is red blood cells.

### 5 BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a typical dialysis tubing connection circuit.

FIG. 2 illustrates a plot of % $\Delta$  Hematocrit (or % $\Delta$  blood volume (BV)) versus Time following an injection of 10 ml saline into the bloodstream at a location upstream of the shunt.

10 FIG. 3 shows a single injection dilutional curve when access recirculation is present, note the second area (curve 2) following the larger first area (curve 1).

FIG. 4 shows a single injection dilutional curve with the arterial and venous tubing lines reversed causing forced (or reversed) recirculation.

15 FIG. 5 diagrammatically represents the dialysis circuit in terms of mass flow, in normal arterial, venous line orientation.

FIG. 6 diagrammatically represents the dialysis circuit in terms of mass flow with arterial and venous lines reversed.

### DETAILED DESCRIPTION OF THE INVENTION

In a preferred embodiment, measurements are conducted using the apparatus  
20 described in U.S. Patent Nos. 5,456,253 and 5,372,136, which are incorporated herein as if reproduced in full below. Both of these patents form part of the present disclosure.

Thus, in a preferred embodiment, hematocrit is measured through blood in a flow

through cuvette located in the access line. In a preferred embodiment, the apparatus and signal manipulations described in U.S. Patent No. 5,372,136 are used to measure hematocrit. The numbered components are the same as FIG. 1 in U.S. Patent No. 5,456,253.

5       In hemodialysis, blood is taken out of a patient 200 by an intake catheter means, one example of which is shown in FIG. 1 as an input catheter 122. Input catheter 122 is intravenously inserted into patient 200 at a site 180 and is used for defining a blood passageway upstream of a blood filter used to filter the impurities out of the blood. The blood filter is also called a dialyzer 130. The unclean blood flows from an artery in patient 200 to a pump means, an example of which is pump 140. From pump 140, the blood flows to dialyzer 130. Dialyzer 130 has an input port 230 and an output port 240. The pump 140 performs the function of moving the unclean blood from patient 200 into input port 230, through dialyzer 130, and out of dialyzer 130 at output port 240.

10      15

Specifically, unclean blood in input catheter 122 is transported to input port 230 of dialyzer 130. After passing through and being cleansed by dialyzer 130, the blood may receive further processing, such as heparin drip, in hemodialysis related component 300. The now clean blood is returned to patient 200 after the dialyzing process by means of an output catheter means, an example of which is output catheter 124. Output catheter 124, which is also intravenously inserted into patient 200 at site 180, defines a blood passageway which is downstream from dialyzer 130, taking the blood output by dialyzer 130 back to patient 200.

20

As mentioned, the hemodialysis process uses a blood filter or dialyzer 130 to

clean the blood of patient 200. As blood passes through dialyzer 130, it travels in straw-like tubes (not shown) within dialyzer 130 which serve as membrane passageways for the unclean blood. The straw-like tubes remove poisons and excess fluids through a process of diffusion. An example of excess fluid in unclean blood is water and an example of poisons in unclean blood are blood urea nitrogen (BUN) and potassium.

The excess fluids and poisons through an ultrafiltration process are removed by a clean dialysate liquid fluid, which is a solution of chemicals and water. Clean dialysate enters dialyzer 130 at an input tube 210 from a combined controller and tank 170. The dialysate surrounds the straw-like tubes in dialyzer 130 as the dialysate flows down through dialyzer 130. The clean dialysate picks up the excess fluids and poisons passing through the straw-like tubes, by diffusion, and then returns the excess fluids and poisons with the dialysate out of dialyzer 130 via an output tube 220, thus cleansing the blood. Dialysate exiting at output tube 220 after cleansing the blood may be discarded.

In some, unclean blood flows from an artery in patient 200 to pump 140 and then to dialyzer 130. Unclean blood flows into dialyzer 130 from input catheter 122 and clean blood flows out of dialyzer 130 via output catheter 124 back to patient 200.

Installed at either end of dialyzer 130 is a spectrophotometry means for defining a blood flow path, for emitting radiation into the blood in the flow path, and for detecting radiation passing through both the blood and the flow path. The spectrophotometry means includes a cuvette means for defining the blood flow path, and an emitter/detector means for emitting and detecting radiation. Within the emitter/detector means is both an emission means for directing radiation and a detector means for detecting radiation.

In a prior art embodiment as shown in FIG. 1, an example of the emitter/detector means is depicted by the emitter/detector apparatus 100. An example of the emission means is indicated by a photoemitter 102. Emitter/detector apparatus 100 also has a detection means, an example of which is depicted as a photodetector 104. An example of the cuvette means is shown in FIG. 1 as cuvette 10.

5 Emitter/detector apparatus 100 enables the detection by photodetector 104 of the portion of radiation which is directed by photoemitter 102 to cuvette 10 and passes through both the blood therein and cuvette 10.

As shown in FIG. 1, a cuvette 10 is installed at either end of dialyzer 130. Each  
10 cuvette 10 has a photoemitter 102 and a photodetector 104 thereon. In the preferred embodiment of the system, photoemitter 102 and photodetector 104 are shown as being held together by a spring loaded C-Clamp type in emitter/detector photo apparatus 100.

The emitter/detector means is electrically connected to a calculation means. In a preferred embodiment of the system, an example of the calculator means is depicted in  
15 FIG. 1 as computer 150 which is electrically connected to photoemitter 102 and photodetector 104 on emitter/detector apparatus 100 by means of cable 120 or 128.

Intake catheter 122 takes blood to cuvette 10 situated before input port 230 of dialyzer 130. Emitter/detector apparatus 100 at input port 230 of dialyzer 130 subjects the blood therein to radiation wavelengths of electromagnetic radiation for the purposes  
20 of analysis, via spectrophotometry, so that the concentration of a desired biological constituent can be derived. Each photodetector 104, at both input port 230 and output port 240 of the dialyzer 130, communicates the detected radiation via cable 120 or 128

to computer 150.

Computer 150 calculates both before dialysis (via cable 120) and after dialysis (via cable 128) concentrations of the sought-after or desired biologic constituent. Computer 150 then displays, respectively, at a first display 152 and a second display 154, the derived concentration of the biological constituent in either analogue or digital representations. The calculation means, shown here by example as computer 150, preferably has the multiple capability of simultaneous real-time computation and display of several blood parameters of interest.

10 1. Single Injection Dilutional Technique.

In the first aspect, approximately 10 mls of saline is injected over five seconds into the arterial line. The measuring disposable blood chamber 10 is immediately downstream (in the arterial line) from the injection point 15, see FIG. 1. A change in hematocrit (AH) instantly occurs due to the dilution of the whole blood by the saline. Then, by appropriately measuring and computing the area under the dilution curve, see FIG. 2, (the Ficke principle), the dialyzer blood flow ( $Q_i$ ), access recirculation (AR), and access blood flow ( $Q_a$ ) are determined in the following manner.

$$Q_i = V / K \int (\% \Delta H) dt \quad (1)$$

where:

20  $Q_i$  = Dialyzer blood flow rate, in ml/min

$K$  = a conversion factor, determined empirically to convert percent change hematocrit units to area and minute units.

$\int (\% \Delta H) dt$  = area under the hematocrit dilution curve (1) in Fig. 3.

V = Volume of saline injected (typically 10 ml)

If access recirculation (AR) is present, FIG. 3 is obtained. In order to determine AR the following equation is used:

5

$$AR = (\int (\% \Delta H)_2 dt / \int (\% \Delta H)_1 dt) \cdot 100 \quad (2)$$

where:

AR = % Access Recirculation, when ultrafiltration is off

$\int (\% \Delta H)_2 dt$  = area under curve 2, the "measuring area"

10  $\int (\% \Delta H)_1 dt$  = area under curve 1, the "calibration area"

The area under the dilution curve 1, the "calibration area", represents 100% of the 10 ml saline bolus passing through the chamber and diluting the blood in the path of the optical detector. The area under dilution curve 2, the "measuring area", represents the 15 amount of saline which "recirculated" from the venous line into the shunt (or access) and "back again" to the arterial line and hence, passing the optical detector a second time.

The areas under the dilution curves are measured during specific time intervals in the following way. With reference to FIG. 3, the injection of saline solution takes place at time 0 seconds. The slope of the resulting line 51 remains essentially flat until about 19 seconds, where there is a dramatic increase in the slope of line 51. It is at this point that the system starts to measure the area under curve 1. The system continues to 20

measure the area under curve 1 until the slope of line S1 changes from a negative slope to a zero slope or a positive slope which occurs at about 41 seconds. It is at that point in time that the measurement of curve 1 stops and the measurement of the area of curve 2 begins. The measurement of curve 2 continues until a time is reached where the slope of line S1 changes from a negative to a zero, which in FIG. 3 occurs at about 78 seconds.

5 It is at this point in time that the measurement of the area of curve 2 stops.

Knowing  $Q_i$  (in ml/min) and the time interval ( $T$ ) between dilution curves 1 and 2 of FIG. 3, the priming dialyzer circuit volume (PDCV) can be calculated with the following:

10

$$PDCV = Q_i T (1/60) \quad (3)$$

Finally, to calculate the access blood flow, the arterial line is reversed with the venous line and placed "downstream" of the venous line in the shunt. A 10 ml saline bolus (given over 5 seconds) is then injected, into the arterial line, as usual, resulting in the dilution curves seen in FIG. 4. As in the determination of access recirculation, the reversed access recirculation (RAR) is computed from the following formula:

15

$$RAR = \int (\% \Delta H)_2 dt / \int (\% \Delta H)_1 dt \quad (4)$$

20 and, as in equation 2, ultrafiltration is off.

Once RAR is determined, then the access blood flow,  $Q_a$ , is calculated from:

$$Q_s = Q_i(RAR^{-1} - 1) \quad (5)$$

Hence, with a single injection of saline into the arterial line, immediately  
5 upstream from the measuring disposable blood chamber, the calibration area (curve 1)  
and the measuring area (curve 2) are obtained, see FIGS. 3 and 4. A reference, or the  
calibration area, is already incorporated within the single injected saline bolus, without  
the need for dual sensors, or a customary second saline injection; where one injection is  
for reference measurements and the second injection is the measuring injection.

10 The single saline injection technique utilizing a single detector is a major  
enhancement and has many advantages. For example, in other methods typically two  
detectors must be "tuned" exactly the same. In a double injection technique, two separate  
injections must be the exact same volume each time and given at the same rate of  
injection, otherwise the calibration areas and the measuring areas will be different, giving  
15 erroneous results.

The equation mentioned above requires accurate measurement of the area under  
the hematocrit dilution curve,  $\int (\% \Delta H) dt$ . The most common error in that measurement  
comes from the variations in the rate of injection of the saline bolus (typically 10ml over  
5 seconds). The actual rate of saline injection can be calculated from time base  
20 parameters seen in the arterial injection. The resulting variation (or perturbation),  $Q_s$ ,  
caused by these injection-induced transients is compensated for as seen in equations 5a  
and 5b (from equation 1):

$$Q_i (\text{corrected}) = V / [K(\text{Area}_m - \text{Area}_p)] \quad (5a)$$

where:  $\text{Area}_m$  = Area measured under the hematocrit dilution curve

$\text{Area}_p$  = Area of push rate of the saline injection

$$\text{Area}_p = [(-0.018)Q_i(\text{raw}) + 1.22] \left[ \frac{211}{\text{span}} - Q_i(\text{raw})(0.3661) \right] \quad (5b)$$

where:  $Q_i(\text{raw})$  = raw blood flow rate based on  $\text{area}_m$

span = time interval from the start of the saline injection to the end of the injection, in seconds.

The injection rate-induced transients can thusly be compensated for resulting in more accurate blood flow, access recirculation and access blood flow measurements.

15 2. The Second Aspect, the  $\Delta$  Hematocrit Technique.

Referencing FIG. 5, the following mathematics allows determination of access recirculation via the  $\Delta$  Hematocrit technique, wherein the following mass (m) and blood flow rate (Q) balance obtains:

$$m_s + m_r = m_i \quad (6)$$

and

$$Q_s + Q_r = Q_i \quad (7)$$

so:

$$Q_i H_s + Q_r H_o = Q_i H_i \quad (8)$$

25 (where  $Q_o = Q_i - UFR$ )

since:

$$\begin{aligned} Q_i H_i &= Q_o H_o \\ &= (Q_i - UFR) H_o \end{aligned} \quad (9)$$

and

$$H_o = (Q_i / (Q_i - UFR)) H_i \quad (10)$$

But since:  $R = Q_o / Q_i$ , dividing equation 8 by  $Q_i$  obtaining:

$$H_i / H_o = (1 - R) [1 - R (Q_i / (Q_i - UFR))]^{-1} \quad (11)$$

Therefore to determine access recirculation (AR) by the  $\Delta$  Hematocrit method the following obtains:

$$AR = 100 \cdot (H_i - H_o) [(Q_i / (Q_i - UFR)) H_i - H_o]^{-1} \quad (12)$$

From Equation 12 note that by either changing the dialyzer blood flow rate,  $Q_i$ , or by changing the ultrafiltration rate (UFR) a change in the hematocrit is created; hence, the direct measurement of access recirculation is determined.

To determine the access blood flow,  $Q_a$ , by the  $\Delta$  Hematocrit method refer to FIG. 6, which shows the arterial and venous lines reversed. Since there must be a hematocrit balance around the tubing/dialyzer circuit the following applies:

$$Q_a H_a + Q_o H_o = H_i (Q_a + Q_o) \quad (13)$$

$$but, Q_i H_i = Q_o H_o, \text{ (and } Q_o = Q_i - UFR\text{)} \quad (14)$$

$$\text{so. } Q_a H_a + Q_i H_i = H_a (Q_a + Q_i - UFR) \quad (15)$$

$$\text{and } H_a / H_i = Q_a (Q_a - UFR) \quad (16)$$

$$\text{Therefore: } Q_a = H_a (UFR) / (H_i - H_a) \quad (17)$$

5 From Equation 17,  $Q_a$ , by the  $\Delta$  Hematocrit technique, is independent of the dialyzer blood flow rate,  $Q_i$ . Therefore, by merely changing the ultrafiltration rate (UFR), access blood flow is directly computed.

By way of example, the value of  $Q_a$  is determined in the following manner. Assume that UFR = 0 milliliters/minute or ml/min. According to equation (17),  $Q_a$  would equal 0 ml/min. Also with UFR = 0 ml/min, the access hematocrit  $H_a$  is measured to be 30.0. This becomes the baseline value for  $H_a$ . When the UFR is increased, as for example, to 30 ml/min, the value of the hematocrit in the arterial line,  $H_i$ , measured after a short period of time, (3 or 4 minutes) is about 31.0. Therefore, according to equation 17,  $Q_a = 31 (30) / (31 - 30) = 930 \text{ ml/min}$ .

15 Utilizing the instantaneous hematocrit monitor, the above  $\Delta$  Hematocrit method will measure AR and  $Q_a$  immediately and directly. Using the  $\Delta$  Hematocrit method with a blood volume monitor (a relative measure of hematocrit) to measure AR and  $Q_a$  will yield immediate and direct results. However, because of the relative measure of hematocrit, the results will not be accurate.

20 It should be emphasized again that while U.S. Pat. No. 5,372,136 shows the measurement of absolute hematocrit, this technique and method described in the second aspect of the invention is intended to incorporate the relative measure of hematocrit

( $\Delta BV$ ), as well as the usage of single wavelength optical, conductimetric or ultrasonic methods of BV measurements. Therefore, the method of simply changing Qi or UFR in order to measure AR or simply changing UFR to measure the Q<sub>s</sub> are important new and unique concepts.

5       U.S. Pat. No. 5,372,136 clearly defines the operational means whereby the instantaneous and continuous measurement of hematocrit is obtained and used in connection with the disposable blood chamber mentioned above.

10      Although the foregoing discussion relates to noninvasive analysis of hemodynamic access flow information, it will be appreciated that the above mentioned circuitry and algorithms may be adapted for analysis of other rheologic parameters.

The present invention may be embodied in other specific forms without departing from its intent or essential characteristics. The described embodiments are to be considered in all respects only as illustrative and not restrictive.

**IN THE CLAIMS:**

1. A method for measuring access recirculation in a dialysis system having arterial and venous tubing lines, said method comprising the steps of:

ensuring that ultrafiltration is off;

introducing a predetermined amount of saline into an injection site in the arterial line over a predetermined period of time;

measuring the percentage change in hematocrit over a first period of time;

measuring the percentage change in hematocrit over a second period of time taking place after the first period of time; and

comparing the measured change in hematocrit over the second period of time to the measured change in hematocrit over the first period of time to yield a signal that is directly proportional to access recirculation.

2. The method for claim 1, further comprising the steps of:

measuring the area ( $\text{Area}_m$ ) under a curve that is indicative of the percentage change in hematocrit over the first and second periods of time;

determining the uncorrected blood flow rate ( $Q_i(\text{raw})$ );

5 determining the area of push rate of the solution injection ( $\text{Area}_p$ ) as a function of  $Q_i(\text{raw})$  and span where span equals the time interval from the start of the saline injection to the end of the injection, in seconds;

measuring the volume of the injected saline;

dividing the volume of the injected saline by ( $\text{Area}_m - \text{Area}_p$ ) times a conversion

factor to yield a result that is indicative of the corrected blood flow rate.

3. The method of claim 2, wherein the uncorrected blood flow rate ( $Q_i$  (raw)) is determined from the  $Area_{\text{m}}$  value.

4. The method of claim 2, wherein the step of determining the  $Area_p$  includes solving the formula  $Area_p = [(-0.018) Q_i \text{ (raw)} - 1.22] [-(2013/\text{span}) - Q_i \text{ (raw)}(0.3661)]$ .

5. The method of claim 1 further comprising the steps of:  
multiplying the signal by a predetermined factor to yield percentage change in access recirculation.

6. The method of claim 5, wherein said factor is 100.

7. The method of claim 1, further comprising the step of locating a blood chamber in the arterial line downstream from the point of introduction of the saline into the arterial line; and

carrying out each of the two measuring steps by photometrically measuring hematocrit for the blood passing through the chamber.

8. A method for measuring dialyzer blood flow in a dialysis system having arterial and venous tubing lines, said method comprising the steps of:

introducing a predetermined amount of saline into the arterial line over a predetermined period of time;

measuring the percentage change in hematocrit over a first period of time;

comparing the volume of saline introduced to the product of the measured change in hematocrit over the first period of time and a predetermined conversion factor to yield a signal that is indicative of dialyzer blood flow rate.

9. A method for measuring priming dialyzer circuit volume in a dialysis system having arterial and venous tubing lines, said method comprising the steps of:

introducing a predetermined amount of saline into the arterial line over a first period of time;

measuring the percentage change in hematocrit over a second period of time;

measuring the percentage change in hematocrit over a third period of time;

comparing the volume of saline introduced into the arterial line to the product of the measured change in hematocrit over the first period of time and a predetermined conversion factor to yield a signal that is indicative of dialyzer blood flow rate;

multiplying the dialyzer blood flow rate by the sum of the first, second and third periods of time and dividing the result by 60 to yield a signal that is indicative of the priming dialysis circuit volume.

10. A method for measuring access blood flow in a dialysis system having arterial and venous tubing lines, said method comprising the steps of:

introducing a predetermined amount of saline into the venous line over a first period of time;

determining dialyzer blood flow rate;

measuring the percentage change in hematocrit over a second period of time;

5 measuring the percentage change in hematocrit over a third period of time;

comparing the measured change in hematocrit over the third period of time to the measured change in hematocrit over the second period of time to yield a signal that is directly proportional to reversed access recirculation (RAR);

subtracting the 1 from the inverse of the RAR and multiplying that result by the dialyzer blood flow rate to yield a signal indicative of access blood flow rate.

11. A method for eliminating injection-induced transients when injecting a solution into an arterial or venous line, the method comprising the steps of:

ensuring that ultrafiltration is off;

5 introducing a predetermined amount of a solution into at least one of the arterial and venous lines over a predetermined period of time;

measuring the area ( $\text{Area}_{\text{m}}$ ) under a curve that is indicative of the percentage change in hematocrit over a period of time;

determining the uncorrected blood flow rate ( $Q_{\text{u}}(\text{raw})$ );

10 determining the area of push rate of the solution injection ( $\text{Area}_{\text{p}}$ ) as a function of  $Q_{\text{u}}(\text{raw})$  and span where span equals the time interval from the start of the solution injection to the end of the injection, in seconds;

measuring the volume of the injected solution;

dividing the volume of the injected solution by ( $\text{Area}_{\text{m}} - \text{Area}_{\text{p}}$ ) times a conversion factor to yield a result that is indicative of the corrected blood flow rate.

12. The method of claim 11, wherein the uncorrected blood flow rate ( $Q_i$  (raw)) is determined from the  $\text{Area}_{\text{m}}$  value.

13. The method of claim 11, wherein the step of determining the  $\text{Area}_{\text{m}}$  includes solving the formula  $\text{Area}_{\text{m}} = [(-0.018) Q_i \text{ (raw)} + 1.22] [- (2013/\text{span}) + Q_i \text{ (raw)}(0.3661)]$ .

14. A method for determining access blood flow in a dialysis system having arterial and venous tubing lines, said method comprising the steps of:

introducing a predetermined amount of saline into an injection site in the venous line over a predetermined period of time;

5 selecting an initial ultrafiltration rate (UFR);

determining the access hematocrit at the initial UFR;

changing the value of the UFR to a second UFR;

measuring the arterial hematocrit at the second UFR;

multiplying the arterial hematocrit by the second UFR and dividing the result by the arterial hematocrit minus the access hematocrit to compute the access blood flow.

15. A method for determining percentage access recirculation (AR) in a dialysis system having arterial and venous tubing lines, said method comprising the steps of:

- introducing a predetermined amount of saline into an injection site in the arterial line over a predetermined period of time;
- 5 selecting an initial ultrafiltration rate (UFR);
- measuring an initial dialyzer blood flow rate ( $Q_i$ );
- determining the access hematocrit ( $H_a$ ) at either the initial UFR or the initial dialyzer blood flow rate;
- 10 changing one of the UFR or the dialyzer blood flow rate to a second value;
- measuring the arterial hematocrit ( $H_a$ ) at the second value;
- computing percentage access recirculation (AR) as a function of a change in either the UFR or the dialyzer blood flow rate.

16. The method of claim 15, wherein said step of measuring dialyzer blood flow comprises the steps of:

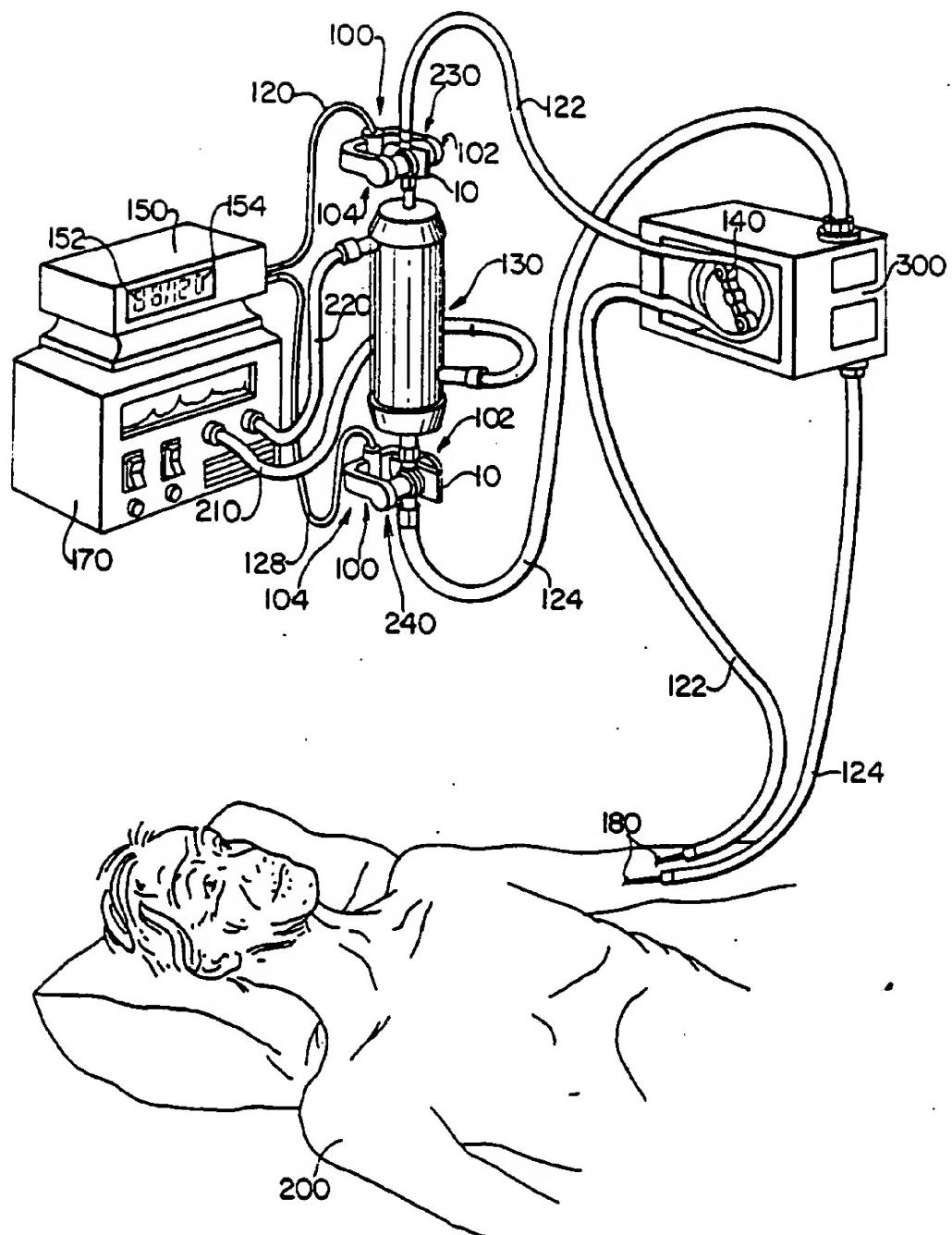
- measuring the percentage change in hematocrit over a first period of time;
- comparing the volume of saline introduced to the product of the measured change in hematocrit over the first period of time and a predetermined conversion factor to yield a signal that is indicative of dialyzer blood flow rate.

17. The method of claim 15, said step of computing percentage access

recirculation comprises the steps of:

solving the equation  $AR = 100(H_i - H_o)[(Q/Q_i - UFR)] H_i - H_u^{-1}$ .

FIG. 1



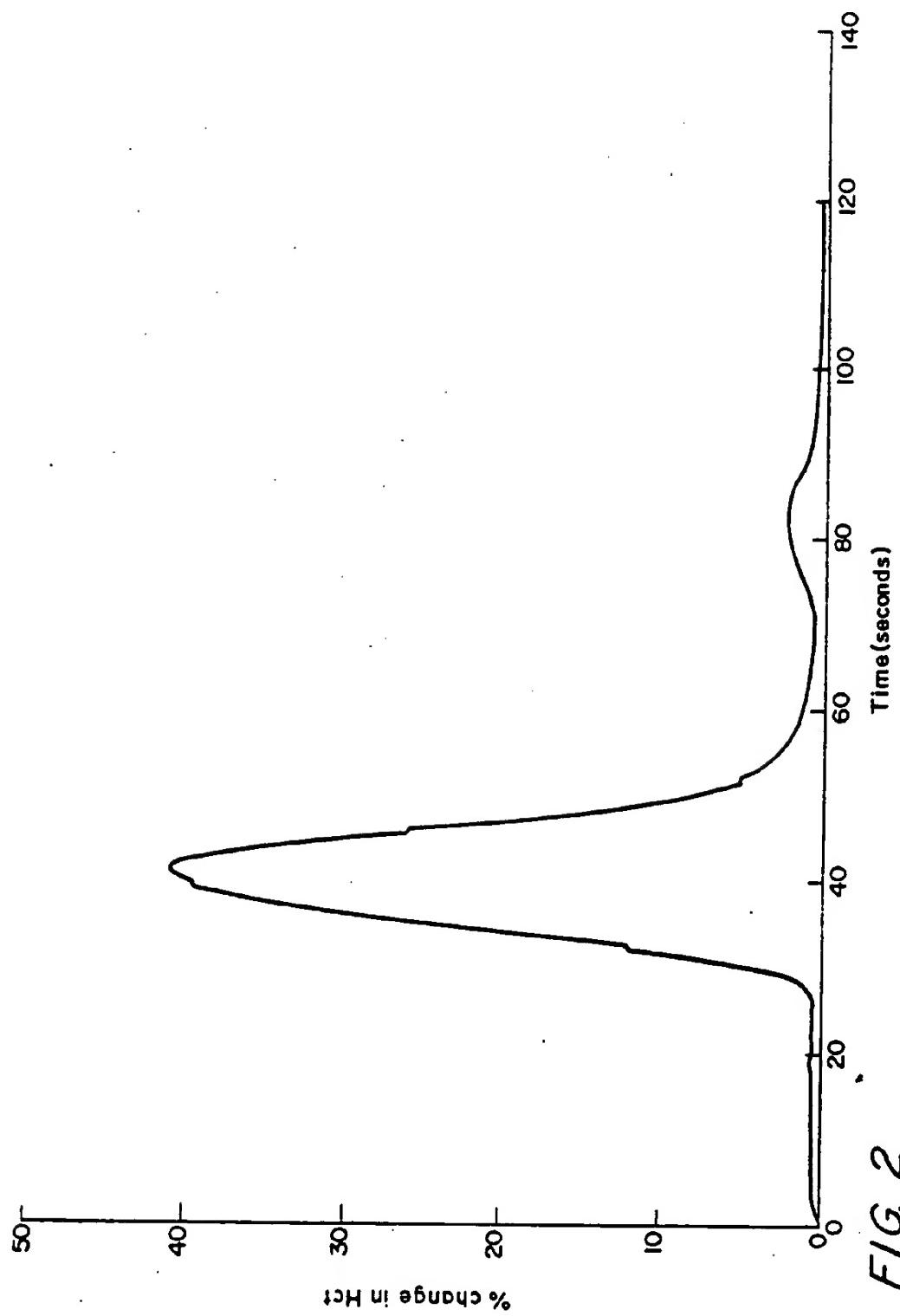


FIG. 2

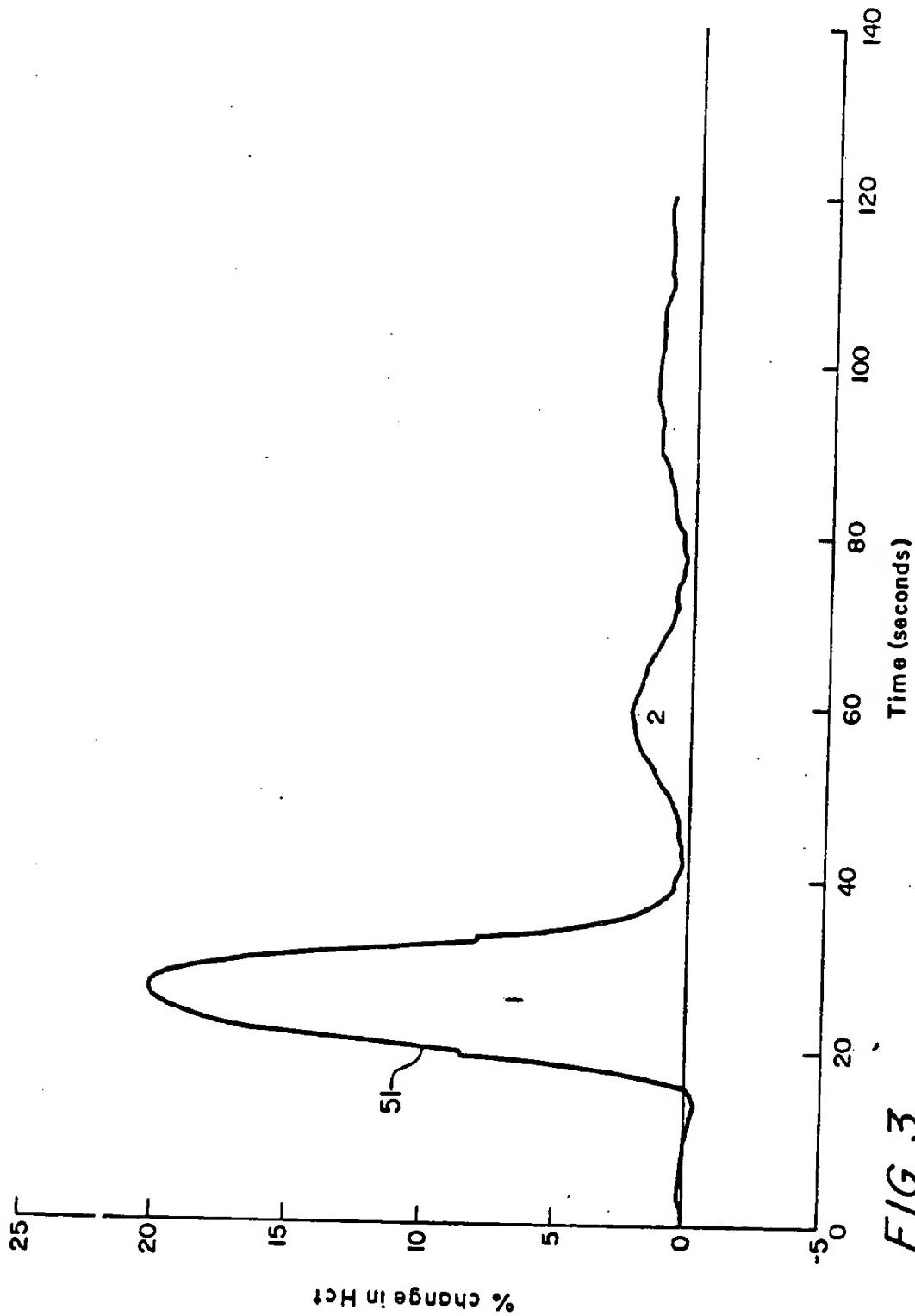


FIG. 3

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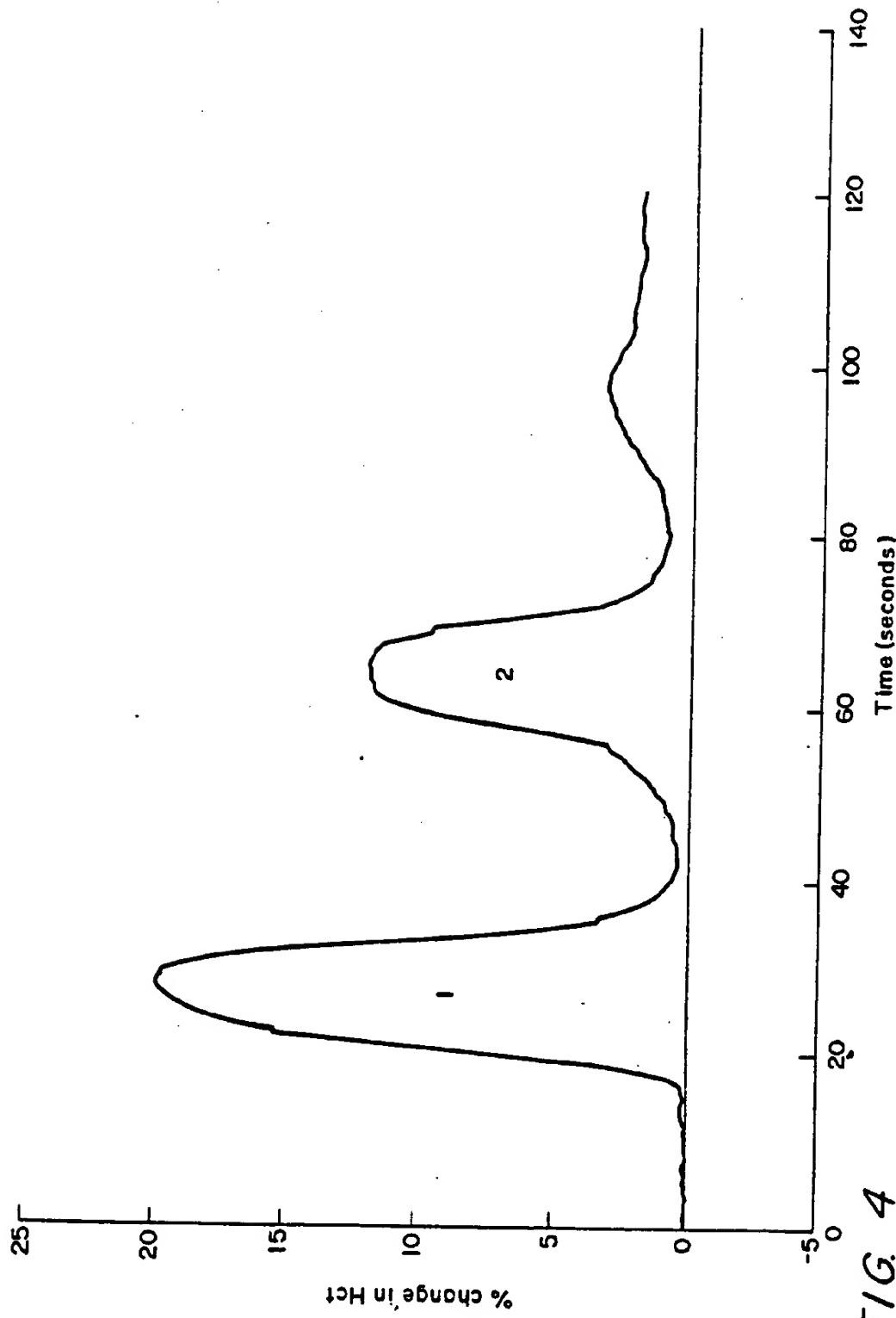
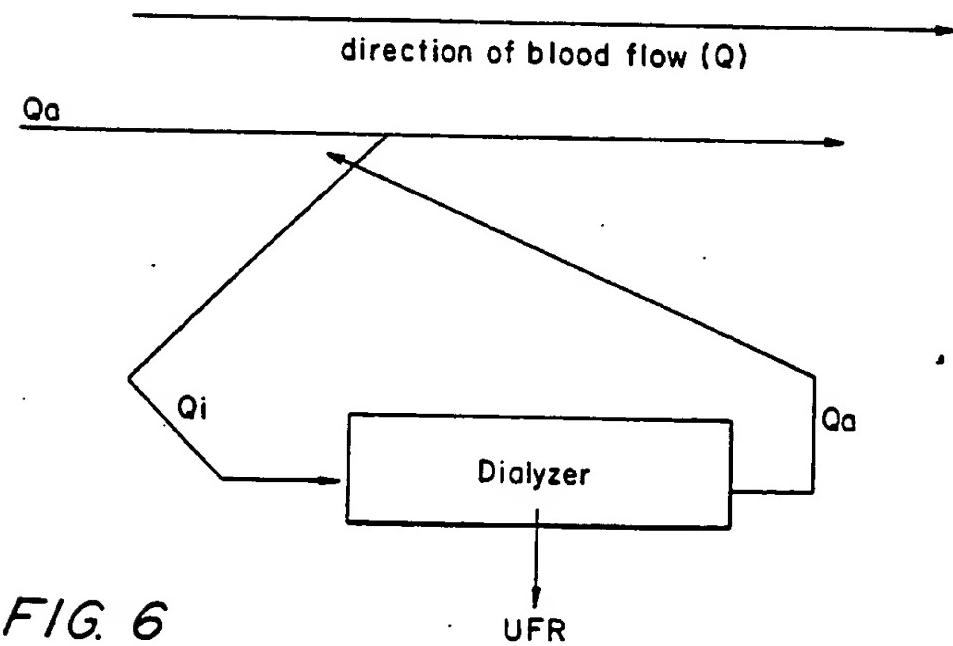
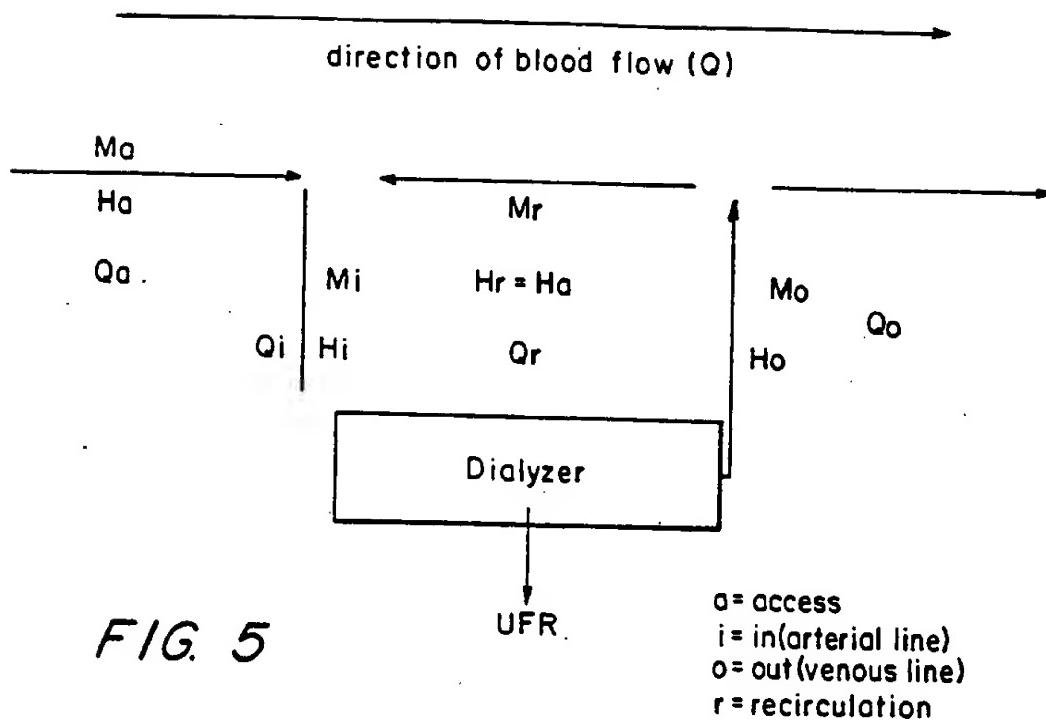


FIG. 4

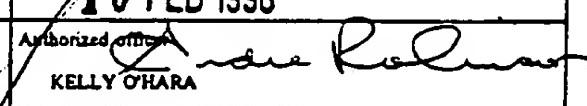
NMT01163



Reversed arterial and venous lines

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US97/19511

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
IPC(6) A61B 19/00 US CL 128/898; 600/326, 476 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols) U.S. : 128/898; 600/326, 476		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) APS, MEDLINE, STN, DIALOG		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US 5,662,806 A (KESHAVIAH et al.) 02 September 1997, entire document.	1-17
Y	US 5,518,623 A (KESHAVIAH et al.) 21 May 1996, entire document.	1-17
Y	US 5,507,723 A (KESHAVIAH et al.) 16 April 1996, entire document.	1-17
Y	US 5,372,136 A (STEUER et al.) 13 December 1994, entire document.	1-17
A	US 4,446,871 A (IMURA) 8 May 1984, entire document.	1-17
A	US 5,442,969 A (TROUTNER et al.) 22 August 1995, entire document.	1-17
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
<ul style="list-style-type: none"> <li>* Special categories of cited documents:</li> <li>"A" document defining the general state of the art which is not considered to be of particular relevance</li> <li>"B" earlier document published on or after the international filing date</li> <li>"C" document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reasons (as specified)</li> <li>"D" document referring to an oral disclosure, use, exhibition or other events</li> <li>"E" document published prior to the international filing date but later than the priority date claimed</li> </ul>		
Date of the actual completion of the international search  17 JANUARY 1998		Date of mailing of the international search report  10 FEB 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230		Authorized officer  KELLY O'HARA Telephone No. (703) 308-0780